**Amendments to the Specification:**

Please replace the paragraph at page 2, lines 16-25, with the following amended paragraph:

Hematopoietic stem cells are responsible for sustaining blood cell production over the life of an animal. The small population of hematopoietic stem cells is sufficient to produce all the mature blood cells in a healthy ~~individuals~~ individual; however, some unhealthy individuals suffer from a lack of a sufficient number of progenitor cells and/or mature blood cells. For example, cancer patients receiving chemotherapeutic or radiotherapy treatments designed to kill the rapidly dividing cancer cells also suffer from the depletion of white blood cells and platelets, thus exposing these patients to life threatening life-threatening opportunistic infections and bleeding episodes. Indeed, this hematopoietic progenitor cell-depleting activity is the dose-limiting factor for most of these chemotherapeutic and radiotherapeutic agents.

Please replace the paragraph at page 3, lines 14-17, with the following amended paragraph:

There are several drawbacks to using chemokines, cytokines, and other immunoregulators as chemoprotectants during the chemotherapeutic or radiotherapeutic treatment of cancer ~~patient~~ patients. These drawbacks include the cost of production and toxicity to the patient.

Please replace the paragraph at page 6, lines 5-11, with the following amended paragraph:

In certain embodiments of the fifth aspect, the FRIL family member molecules [[is]] are immobilized on a solid support. In some embodiments, the solid support is a bead, such as a magnetic bead. In some embodiments, the unbound cells are separated by applying a magnet to the population of cells contacted with the FRIL family member molecules immobilized on the magnetic bead. In further embodiments, the population of cells bound to the FRIL family

member molecules immobilized on a magnetic bead is rinsed with a physiologically acceptable solution while the magnet is applied.

Please replace the paragraph at page 6, lines 16-19, with the following amended paragraph:

In preferred embodiments of the fifth aspect of the invention, the isolated population of progenitor cells is a population of hematopoietic progenitor [[cell]] cells. In various embodiments, the population of cells is whole blood, umbilical cord blood, bone marrow cells, or fetal liver cells.

Please replace the paragraph at page 6, lines 25-29, with the following amended paragraph:

In a sixth aspect, the invention provides an isolated population of progenitor cells isolated by a method comprising contacting a population of cells with a plurality of FRIL family member molecules, and separating the unbound cells, wherein the cells bound to the FRIL family member molecules are an isolated population of progenitor cell. Preferably, the progenitor cell is from a human.

Please replace the paragraph at page 7, lines 1-6, with the following amended paragraph:

In certain embodiments of the sixth aspect, the cells of the isolated population do not express CD34. In certain embodiments, the cells of the isolated population express a receptor tyrosine kinase selected from the group consisting of [[from]] FLK1, FLT1, FLT3, FLT4, and Kit. In some embodiments, the cells of the isolated population express a cell surface molecule selected from the group consisting of CD11b and CD11c. In preferred embodiments, the cells of the isolated population express FLT3.

Please replace the paragraph at page 13, lines 15-21, with the following amended paragraph:

Figures 19A and 19B are representations of line graphs showing the biological specificity of receptor-transfected 3T3 cells. Figure 19A shows that rhM-CSF specifically stimulated Fms 3T3 (solid circles) but ~~not either~~ neither mFlt3/Fms 3T3 (open circles) [[or]] nor parent 3T3 cells (solid squares) in biological screening assay in a dose-dependent manner. Figure 19B shows that PHA-LCM (reciprocal dilution) stimulated mFlt3/Fms 3T3 (solid circles) and Stk 3T3 (open circles) but not parent untransfected 3T3 cells (solid squares).

Please replace the paragraph at page 14, lines 23-26, with the following amended paragraph:

Figure 24B shows a direct amino acid sequence comparison of Pv-FRIL (SEQ ID NO:56), a representative, non-limiting FRIL family member of the invention, with ~~Dl-FRIL, another representative, non-limiting FRIL family member of the invention~~ DLL (SEQ ID NO:55), the mannose binding lectin of Gowda et al., and the PHA lectin, PHA-E (SEQ ID NO:57).

Please replace the paragraph at page 15, lines 4-11, with the following amended paragraph:

Figures 27A-27B are representations of line graphs showing the total cell numbers and progenitor levels in the presence of Dl-FRIL,a representative, non-limiting FRIL family member of the invention, or cytokines. Enriched CB $CD34^+$ cells were cultured for ~~3,6,10, or 13 days~~ 3, 6, 10, or 13 days in the presence of Dl-FRIL (solid symbols) or cytokines (open symbols). Colonies were scored on day 14 and progenitor levels were calculated based on total cell numbers. Values shown represent the mean±SEM of data from up to 10 experiments. Figure 27A shows the total cell numbers over time. Figure 27B shows the progenitor levels in cultures over time.

Please replace the paragraph at page 15, lines 12-23, with the following amended paragraph:

Figures 28A-28D are representations of line and bar graphs showing the total cell numbers and progenitor levels first in the presence of Dl-FRIL, a representative, non-limiting FRIL family member of the invention, and second in presence of cytokines. Figure 28A shows the total numbers of cells cultured with Dl-FRIL for the entire 10 days (solid symbols) or for 6 days followed by 4 days of cytokine stimulation (open symbols). Figure 28B shows the progenitor levels in cells cultured with Dl-FRIL for the entire 10 days (solid symbols) or for 6 days followed by 4 days of cytokine stimulation (open symbols). Figure 28C shows the total numbers of cells cultured with Dl-FRIL for 13 days (solid symbols) or for 10 days followed by 3 days of cytokine stimulation (open symbols). Figure 28D shows the progenitor levels in cells cultured with Dl-FRIL for 13 days (solid symbols) or for 10 days followed by 3 days of cytokine stimulation (open symbols).

Please replace the paragraph bridging pages 15 and 16, with the following amended paragraph:

Figures 29A-29D are representations of representative Southern blot analyses showing the quantitative analysis of SRC after *ex vivo* cultures with ~~Dl-FRIL,a~~ Dl-FRIL, a representative, non-limiting FRIL family member of the invention, or cytokines and after transplantation into mice. Figure 29A is a representation of a representative Southern blot showing human DNA in the marrow of mice transplanted with cells that were cultured with Dl-FRIL for 6 days (lane 1), Dl-FRIL for 10 days (lane 2), or with Dl-FRIL for 6 days followed by 4 days with cytokine stimulation (lane 3). Figure 29B is a representation of a representative Southern blot showing human DNA in the marrow of mice transplanted with cells cultured with Dl-FRIL for 10 days (lanes 1-2), or with Dl-FRIL for 6 days followed by 4 days with cytokine stimulation (lanes 3-4). Figure 29C is a representation of a representative Southern blot showing human DNA in the marrow of mice transplanted with the original cells prior to seeding (lane 1), or with cells

cultured with Dl-FRIL for 13 days (lane 2). Figure 29D is a representation of a representative Southern blot showing human DNA in the marrow of mice transplanted with cells cultured with FRIL for 10 days (lane 1), Dl-FRIL for 6 days followed by 4 days of cytokine stimulation (lane 2), Dl-FRIL for 13 days (lane 3), or with Dl-FRIL for 10 days followed by 3 days of cytokine stimulation (lane 4).

Please replace the paragraph bridging pages 16 and 17, with the following amended paragraph:

Figure 31 is a representation of a representative Southern blotting analysis showing the levels of ~~levels of~~ human cell engraftment in the BM of NOD/SCID $B2M^{null}$ transplanted with $CD34^{+}CD38^{-/low}$ cells cultured in the presence of Dl-FRIL, a representative, non-limiting FRIL family member of the invention. Sorted cells ($2x10^5$ initial cells /treatment) were cultured in the presence of Dl-FRIL for 6 days followed by additional 4 days exposure to cytokines, or with Dl-FRIL alone for 10 days. After 10 days, $3.6x10^5$ cells harvested from cytokine culture were divided and transplanted into 3 mice (lanes 1-3), while $3.5x10^4$ cells harvested from Dl-FRIL alone culture were transplanted to one mouse (lane 4). DNA was harvested from the bone marrow of transplanted mice and subjected to Southern blotting analysis with radiolabeled human chromosome 17-specific $\alpha$-satellite probe (p17H8). A representative experiment out of 4 is shown.

Please replace the paragraph bridging pages 17 and 18, with the following amended paragraph:

Figures 34A-34B are representations of bar graphs showing the growth effect of Dl-FRIL, a representative, non-limiting FRIL family member of the invention, on $CD34^{+}$ cells and progenitors compared to Flt3 ligand and cytokine combinations. (+) indicates co-culture of factors for the entire 10 days while (->) indicates substitution of the first factor after 6 days with cytokines, as indicated under the x axis. Figure 34A shows the total cell numbers. Figure 34B

shows the percentage of CFU-GEMM out of total colonies. Values shown are per $2x10^5$ seeded ~~cells, and~~ cells and represent the mean ± SEM of data from 5 experiments.

Please replace the paragraph at page 18, lines 13-22, with the following amended paragraph:

Figures 36A-36C are representations of line graphs showing the dose response of CB mnc chemotherapeutic agents in the presence and absence of Dl-FRIL, a representative, non-limiting FRIL family member of the invention. Chemotherapy agents were assayed over a 5-log dose range on CB MNC ($2 \times 10^5$ cells /0.1 mL) in AIMV (Life Technologies) containing Agar-SCM (StemCell Technologies). Viable cells were determined after 5 days of culture by XTT. Solid squares indicate chemotherapy drug with no Dl-FRIL; solid triangles indicate cultures containing Dl-FRIL at 10 ng/ml in all wells; and open circles indicate Dl-FRIL in all wells at 100 ng/ml. Figure 36A shows the dose response to Ara-C; Figure 36B shows the dose response to ~~doxorubicin,~~ doxorubicin; and Figure 36C shows the dose response to 5-FU.

Please replace the paragraph at page 19, lines 17-26, with the following amended paragraph:

In a first aspect, the invention provides an essentially pure composition of a member of the FRIL family of progenitor cell preservation factors. The term, "FRIL family of progenitor cell preservation factors" is used to mean a family of lectins, wherein each FRIL family member molecule binds to a normally glycosylated FLT3 receptor, wherein each FRIL family member molecule preserves progenitor cells, and wherein one FRIL family member molecule that is isolated from a hyacinth bean (*i.e., Dolichos lab lab*) has an amino acid sequence which comprises the following eight amino acid sequence: TNNVLQXT (SEQ ID NO: 24). By "FRIL family member" or [[FRIL]] "FRIL family member molecule" is meant one or more molecules of the FRIL family of progenitor cell preservation factors.

Please replace the paragraph bridging pages 19 and 20, with the following amended paragraph:

In accordance with the first aspect of the invention, a composition of a FRIL family member, which includes a mutant of another FRIL family member molecule or a fusion protein comprising a portion derived from a FRIL family member molecule or mutant thereof, wherein each FRIL family member molecule that binds to a normally glycosylated FLT3 receptor has at least about 45% amino acid sequence identity with the amino acid sequence of another member of the FRIL family, preferably at least about 50% identity, even more preferably at least about 55% identity, still more preferably at least about 60% identity, and still more preferably at least about 65% identity with the sequence of the second protein. In the case of proteins having high sequence identity, the amino acid sequence of the first protein shares at least about 75% sequence identity, preferably at least about 85% identity, and more preferably at least about 95% identity, with the amino acid sequence of another member of the FRIL family.

Please replace the paragraph at page 24, lines 3-7, with the following amended paragraph:

Uncommitted progenitor cells, such as hematopoietic stem cells, can be described as being "totipotent," *i.e.*, both necessary and sufficient for generating all types of mature cells. Progenitor cells that retain a capacity to generate all cell lineages, but that ~~can not~~ cannot self-renew, are termed "pluripotent." Cells that can produce some but not all blood lineages and ~~can not~~ cannot self-renew are termed "multipotent."

Please replace the paragraph bridging pages 26-27, with the following amended paragraph:

In accordance with the first aspect of the invention, a FRIL family member molecule may be purified from a natural source by methods well known in the art. For example, the purification of Dl-FRIL from *Dolichos lab lab* is described below in Example 1. The purification

of Pv-FRIL from *Phaseolus vulgaris* as described below in Example 5. The purification of YamFRIL from *Sphenostylis stenocarpa* is described below in ~~Example 22..~~ Example 22. Such methods also include, for example, those described by Moore in PCT application PCT/US97/22486 and by Gowda et al., *supra*. A suitable natural source from which to purify a FRIL family member molecule includes plants, especially legume plants. Legumes, such as the garden pea or the common bean, are plants ("leguminous plants") from a family (*Leguminosae*) of dicotyledonous herbs, shrubs, and trees bearing (nitrogen-fixing bacteria) nodules on their roots. These plants are commonly associated with their seeds (*e.g.*, the garden pea or the common bean)

Please replace the paragraph at page 27, lines 4-11, with the following amended paragraph:

More specifically, a FRIL family member molecule according to the first aspect of the invention can be purified from members of the tribe *Phaseoleae*. For example, a FRIL family member molecule can be purified from *Dolichos lab lab* (*e.g.*, hyacinth beans, which is also known by other common names throughout the world). Alternatively, a FRIL family member molecule can be purified from varieties of the common bean (*Phaseolus vulgaris*) (*e.g.*, red kidney beans and white kidney beans), from the yam bean *(Sphenostylis stenocarpa)* or from *Vigna sinensis*, commonly known as the black-eyed pea.

Please replace the paragraph bridging pages 31-32, with the following amended paragraph:

By a "recombinant nucleic acid" is meant a nucleic acid which encodes a FRIL family member molecule, or a portion encoding at least 15 contiguous amino acids thereof, or a mutant thereof, or a fusion protein comprising the molecule, portion ~~thereof~~ thereof, or mutant ~~thereof~~ thereof, or is capable of expressing an antisense molecule specifically complementary thereto, or a sense molecule that shares nucleic acid sequence identity thereto wherein the recombinant

nucleic acid may be in the form of linear DNA or RNA, covalently closed circular DNA or RNA, or as part of a chromosome, provided however that it cannot be the native chromosomal locus for a FRIL family member molecule. Preferred recombinant nucleic acids of the invention are vectors, which may include an origin of replication and are thus ~~replicatable~~ capable of replication in one or more cell type. Certain preferred recombinant nucleic acids are expression vectors, and further comprise at least a promoter and passive terminator, thereby allowing transcription of the recombinant nucleic acid in a bacterial, fungal, plant, insect or mammalian cell. By "nucleic acid" or "nucleic acid molecule" as used herein, means any deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), including, without limitation, complementary DNA (cDNA), genomic DNA, RNA, hnRNA, messenger RNA (mRNA), DNA/RNA hybrids, or synthetic nucleic acids (*e.g.*, an oligonucleotide) comprising ribonucleic and/or deoxyribonucleic acids or synthetic variants thereof. The nucleic acid of the invention includes, without limitation, an oligonucleotide or a polynucleotide. The nucleic acid can be single stranded, or partially or completely double stranded (duplex). Duplex nucleic acids can be homoduplex or heteroduplex.

Please replace the paragraph bridging pages 32-33, with the following amended paragraph:

A recombinant nucleic acid according to the second aspect of the invention can also be chemically synthesized by methods known in the art. For example, recombinant DNA can be synthesized chemically from the four nucleotides in whole or in part by methods known in the art. Such methods include those described in Caruthers, M.H., *Science* 230(4723):281-285, ~~1985).~~ 1985. DNA can also be synthesized by preparing overlapping double-stranded oligonucleotides, filling in the gaps, and ligating the ends together. See, generally, Sambrook et al., *supra*, and Glover and Hames, eds., *DNA Cloning*, 2d ed., Vols. 1-4, IRL Press, Oxford, 1995.

Please replace the paragraph at page 33, lines 3-7, with the following amended paragraph:

A recombinant nucleic acid molecule of the invention encoding a mutant FRIL family member can be prepared from wild-type DNA by site-directed mutagenesis (see, for example, Zoller and Smith, *Nucleic. Acids. Res.* 10:6487-6500, 1982; Zoller, M.J., *Methods Enzymol.* 100:468-500, 1983; Zoller, M.J., *DNA* 3(6):479-488, ~~1984.;~~ 1984; and McPherson, M.J., ed., *Directed Mutagenesis: A Practical Approach*, IRL Press, Oxford, 1991.

Please replace the paragraph at page 34, lines 13-17, with the following amended paragraph:

Suitable cloning/expression vectors for use in mammalian cells are also known. Such vectors include well-known derivatives of SV-40, adenovirus, and cytomegalovirus (CMV) retrovirus-derived DNA sequences. Any such vectors, when coupled with vectors derived from a combination of plasmids and phage DNA, *i.e.*, shuttle vectors, allow for the isolation and identification of protein coding sequences in prokaryotes.

Please replace the paragraph bridging pages 36 and 37, with the following amended paragraph:

Compositions of FRIL family members may be used safely and efficaciously as a ~~therapeutics~~ therapeutic. The gastrointestinal tracts of animals come in constant contact with lectins, such as FRIL family members, in raw and/or cooked vegetables and fruits. Many lectins pass through the gastrointestinal tract biologically intact (Pusztai, A., *Eur. J. Clin. Nutr.* 47: 691-699, 1993). Some lectins interact with the gut and are transported into the peripheral blood circulation. For example, a recent study found peanut agglutinin (PNA) in the blood of humans at levels of 1-5 μg/ml an hour after ingesting 200 g of raw peanuts (Wang et al., *Lancet* 352: 1831-1832, 1998). Antibodies to dietary lectins are commonly found in people at levels of ~1

μg/ml (Tchernychev and Wilchek, *FEBS Lett.* 397: 139-142, 1996). These circulating antibodies do not block carbohydrate binding of the lectins.

Please replace the paragraph at page 37, lines 23-28, with the following amended paragraph:

A composition of a FRIL family member of the invention and pharmaceutical formulation comprising a composition of a FRIL family member of the invention may be administered to patients having, or predisposed to developing, a condition whereby the patient's hematopoietic progenitor cells are depleted. Such a condition may be congenital. For example, the patient may have severe combined immunodeficiency or aplastic anemia.

Please replace the paragraph at page 38, lines 15-29, with the following amended paragraph:

In certain embodiments, administration of the pharmaceutical formulation of the invention to a patient prior to the treatment of the patient with a therapeutic treatment having a hematopoietic progenitor cell-depleting activity enables treatment of the patient with a higher dosage of the therapeutic treatment. The higher dosage of the therapeutic treatment may be accomplished by either an increased dose of the therapeutic treatment and/or an increased duration of treatment with the therapeutic treatment. For example, a child diagnosed with childhood Acute Myelogenous Leukemia (AML) is typically initially treated for the first seven days with daunorubicin at 45 mg/m$^2$ on Days 1-3 plus Ara-C at 100 mg/m$^2$ for 7 days plus GTG at 100 mg/m$^2$ for 7 days. The same child pretreated with a composition in accordance with this aspect of the invention may be able to tolerate a higher dosage (*i.e.*, higher dose and/or prolonged treatment period) of any or all of these chemotherapeutics. Such an increase in dosage tolerance of a therapeutic ~~treatment(*e.g.*, a chemotherapeutic)~~ treatment (*e.g.*, a chemotherapeutic) having a hematopoietic progenitor cell-depleting activity in a cancer patient is desirable since a higher dosage may result in the destruction of more cancerous cells.

Please replace the paragraph at page 39, lines 1-9, with the following amended paragraph:

The pharmaceutical formulations and/or compositions of the invention may be administered by any appropriate means. For example, the pharmaceutical formulations and/or compositions of the invention may be administered to [[an]] a mammal within a ~~pharmaceutically acceptable~~ pharmaceutically acceptable diluent, carrier, or excipient, in unit dosage form according to conventional pharmaceutical practice. Administration may begin before the mammal is symptomatic for a condition whereby the patient's hematopoietic progenitor cells are depleted. For example, administration of the pharmaceutical formulations of the third aspect of the invention to a cancer patient may begin before the patient receives radiotherapy and/or chemotherapy treatment.

Please replace the paragraph at page 39, lines 24-27, with the following amended paragraph:

In certain embodiments of the third aspect of the invention, the patient is a human or a domesticated animal. By "domesticated animal" is meant an animal domesticated by humans, including, without limitation, a cat, a dog, ~~elephants~~ an elephant, a horse, a sheep, a cow, a pig, and a goat. In some embodiments, the patient has cancer.

Please replace the paragraph at page 40, lines 19-25, with the following amended paragraph:

In a fifth aspect, the invention provides a method for isolating a population of progenitor cells, comprising contacting a population of cells with a plurality of FRIL family member molecules, and separating the unbound cells, wherein the cells bound to the FRIL family member molecules are an isolated population of progenitor cells. "FRIL family member molecule" and "progenitor cell" are as described for the first aspect of the invention. By

"unbound cell" is meant a cell that does not bind to a FRIL family member. "Bind" is [[a]] as described for the first aspect of the invention.

Please replace the paragraph at page 41, lines 10-11, with the following amended paragraph:

In preferred embodiments, the isolated population of progenitor cells is from a human or ~~is from~~ a domesticated animal.

Please replace the paragraph at page 41, lines 12-23, with the following amended paragraph:

In certain embodiments of the fifth aspect of the invention, the FRIL family member molecules are detectably labeled. By "detectably labeled" is meant that the FRIL family member is attached to a label that is detectable visually or instrumentally. Detectable labels such as enzymes and chromophoric molecules can be conjugated to the FRIL family member molecules by means of coupling agents, such as dialdehydes, carbodiimides, and dimaleimides. Numerous methods of labeling proteins are known in the art. The label can also be directly attached through a functional group on the FRIL family member. Such a functional group may be present on the FRIL family member molecule to be detectably labeled; alternatively, the FRIL family member molecules can be modified using standard techniques to contain a functional group. Some examples of suitable functional groups include, without limitation, amino, carboxyl, sulfhydryl, maleimide, isocyanate, and isothiocyanate.

Please replace the paragraph at page 43, lines 11-17, with the following amended paragraph:

Methods for isolating cells that bind FRIL family member molecule-coated magnetic beads are described below in Example 16. Magnetic beads are commerically available (e.g., from Dynabeads Tosylactivated, Lake Success, NY; or from Miltenyi Biotec, Auburn, CA).

Since the FRIL family member is protein, it can be conjugated to a magnetic bead via amino- or sulfhydryl-groups of the protein. A FRIL family member molecule can also be immobilized on magnetic beads by a biotin-strepavidin interaction.

Please replace the paragraph at page 43, lines 18-27, with the following amended paragraph:

Preferred magnetic beads are the MACS super-paramagnetic MicroBeads (from Miltenyi Biotec) which are extremely small, approximately 50 nm in diameter (MACS beads are about one million times smaller in volume than eukaryotic cells). Because MACS beads react like magnetic antibodies, magnetic labeling is achieved within minutes. MACS MicroBeads form a stable colloidal suspension and do not precipitate or aggregate in magnetic fields. Because of their size and composition (iron oxide and polysaccharide) ~~make the~~ MACS beads are biodegradable, so labeled cells retain their physiological function. This property of MACS beads is particularly useful for bead-sorted FRIL family member-binding cells, which bind the FRIL family member with such high affinity that it is difficult to remove the beads.

Please replace the paragraph at page 44, lines 11-14, with the following amended paragraph:

In preferred embodiments of the fifth aspect of the invention, the isolated population of progenitor [[cell]] cells is a population of hematopoietic progenitor cells. In various embodiments, the population of cells is whole blood, umbilical cord blood, bone marrow cells, or fetal liver cells.

Please replace the paragraph at page 46, lines 14-21, with the following amended paragraph:

In certain embodiments of the sixth aspect of the invention, where the cells of the isolated population are hematopoietic progenitor cells, transplantation of the cell into an animal lacking a population of hematopoietic progenitor cells sufficient to enable survival of the animal

reconstitutes the animal, wherein the transplanted animal survives. Determination of the ability of a hematopoietic progenitor cell to reconstitute [[a]] an animal lacking a population of hematopoietic progenitor cells sufficient to enable survival of the animal may be made using the methods described below for the NOD-SCID mouse.

Please replace the paragraph at page 46, lines 22-26, with the following amended paragraph:

In certain embodiments, the hematopoietic progenitor cells are from a mouse or a human and the animal is a mouse. In some embodiments, the mouse is a severe combined immunodeficient (SCID) mouse (*e.g.*, the NOD-SCID mouse described below) or a mouse that has been exposed to a sublethal dose of radiation and/or ~~chemotherapy~~ chemotherapy.

Please replace the paragraph at page 47, lines 11-25, with the following amended paragraph:

In accordance with this aspect of the invention, the terms "effective amount" and "effective period of time" are used to denote known treatments at dosages and for periods of time effective to preserve progenitor cells. Where administered to a patient, preferably, such administration is systemic (*e.g.*, by intravenous injection). Effective amounts and effective periods of time can be determined using the models and assays described herein. For example, the Examples below describe the preservation of progenitor cells that have SCID-reconstituting ability. In accordance with the invention, an effective amount may range from about 0.1 ng/mL to about 1 μg/mL of a FRIL family member, preferably about 1.0 ng/mL to to about 1.0 μg/mL, more preferably about 1.0 ng/mL to about 100 ng/mL, even more preferably about 10 ng/mL to about 50 ng/mL, and most preferably about 50 ng/mL of a FRIL family member in culture. In accordance with the invention, an effective period of time includes culturing the cells in the presence of a FRIL family member for between ~~would include~~ from about 2 hours to 5 days,

more preferably from about 12 hours to about 3 days, and most preferably for about 24 ~~hours..~~ hours.

Please replace the paragraph bridging pages 52 and 53, with the following amended paragraph:

Total RNA was prepared from mid-maturation *Dolichos lab lab* seeds stored at -70° C following the procedure of ~~Pawloski et al.Mol. Plant Biol. Manual 5: 1 - 13, 1994~~ Pawloski et al. *Mol. Plant Biol. Manual* 5: 1-13, 1994). Poly ($A^+$) RNA was obtained from this total RNA using the PolyATract mRNA Isolation System (Promega) according to the manufacturer's instructions. Avian myeloblastosis virus reverse transcriptase (Promega) was used to generate cDNA from 0.5 μg ~~poly($A^+$)RNA~~ poly($A^+$) RNA, or from 3.0 μg of total RNA, using 1 μg of oligo(dT) in standard reaction conditions (Sambrook et al., *Molecular Cloning. A Laboratory Manual*, 2d ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, 1989).

Please replace the paragraph at page 56, lines 10-12, with the following amended paragraph:

The naturally-occurring signal sequence from the FRIL family member isolated from ~~Dolichos lab lab~~ *Dolichos lab lab* (*i.e.*, Dl-FRIL) has the following sequence:
MASSNLLTLA LFLVLLTHAN SA (SEQ ID NO: 4)

Please replace the paragraph at page 65, lines 3-15, with the following amended paragraph:

For immunoblot analysis (Western blot), the purified proteins were separated by SDS-PAGE in general accordance with the method described above. The gel was equilibrated in transfer buffer (25 mM Tris pH 8.3, 192 mM Glycine, 20% MeOH) and blotted onto nitrocellulose (Bio-Rad, Hercules, CA) for 1 hour at 100 V using a Bio-Rad electrotransfer apparatus. Non-specific binding was blocked by incubating the blots for at least 1 hour in 1X

TBS (20 mM Tris pH 7.5, 500 mM NaCl) containing 3% gelatin. Blotting was followed by incubation with a primary antibody (a polyclonal rabbit serum raised against the N-terminal peptide of the β-subunit of *Phaseolus vulgaris* FRIL (*i.e.*, Pv-FRIL), 1:100 dilution, 3 ~~hour~~ hours; described below in Example 5), followed by incubation with a secondary antibody (goat anti-rabbit IgG conjugated to horseradish peroxidase at 1:1000 dilution for 1 hour). The blots were washed and the color developed with the color development reagent (Bio-Rad). A representative result is shown in Fig. 12, with the lanes identified in Table 2, below.

Please replace the paragraph at page 66, lines 4-14, with the following amended paragraph:

Dl-FRIL interacts with the mammalian FLK2/FLT3 tyrosine kinase receptor. A specific and quantitative biological assay using NIH 3T3 fibroblasts transfected either with a chimeric receptor having the extracellular portion of the murine FLT3 receptor combined with the intracellular portion of the human Fms receptor (Dosil et al., *Mol. Cell. Biol.* 13(10):6572-6585 1993) or with the full length human receptor (Small et al., *Proc. Natl. Acad. Sci. USA* 91:459-463, 1994) can be used to evaluate lectin biological activity during purification. Serial two-fold dilutions of lectin samples across rows of a 96 well plate allowed for greater than a thousand-fold range to access FLT3 3T3 biological activity. Either the murine or human FLT3 ligand (FL) (Lyman et al., *Cell* 75:1157-1167, 1993; Hannum et al., ~~Nature~~ *Nature* 368: 643-648, 1994) or the FRIL was found to rescue FLT3-transfected cells from death in this assay.

Please replace the paragraph bridging pages 66 and 67, with the following amended paragraph:

Specifically, 3T3 cells cultured in tissue culture plates (Becton Dickinson Labware, Lincoln Park, NJ) were removed from the plates by washing cells twice in Hank's buffered saline solution (HBSS; Gibco Laboratories, Grand Island, NY). Non-enzymatic cell dissociation buffer (Gibco) was added for 15 minutes at room temperature. The resulting cells [[wee]] were

washed in medium. FLT3 3T3 cells were cultured at a final concentration of 3,000 cells per well in a volume of 100 μL of serum-defined medium containing 10 mg/mL rhIL1-α, 10% AIMV (Gibco, Grand Island, NY) and 90% Dulbecco's modification of Eagle's medium (DMEM; Gibco) in 96 well plates. Under these assay conditions, cells die after two to four days of culture in a humidified incubator at 37°C and 5% $CO_2$ unless exogenously added ligand rescues cells from death. Each 96 well plate contained wells of cells containing calf serum, which stimulates all 3T3 cells, as a positive ~~controls~~ control and wells of cells containing medium only as a negative control ("blank"). Full-length Fms-transfected 3T3 cells (biological response shown in Tessler et al., *J. Biol. Chem.*, 269:12456-12461, 1994) served as receptor-transfected control target cells, and parent 3T3 cells served as untransfected control cells. Proliferation and cell survival was quantitated by addition of XTT (~~2,3-bis~~ 2, 3-bis [Methoxy-4-nitro-5sulfophenyl]-2H-tetrazolium-5 carboxanilide inner salt) (Diagnostic Chemicals Ltd, Charlottetown, Prince Edward Island, Canada), which is a tetraformazan salt cleaved by actively respiring cells (Roehm et al., *J. Immunol. Methods* 142: 257-265, 1991). Proliferation and cell survival was quantitated spectrophotometrically using a Vmax kinetic plate reader (Molecular Devices Corp., Mountain View, CA), and recorded as either relative activity (units/mL) or as specific activity (units/mg). One unit of biological activity was defined as the reciprocal dilution at which half-maximal stimulation of cells is detected.

Please replace the paragraph bridging pages 82 and 83, with the following amended paragraph:

Both primary and secondary PCR reactions were performed in 100 μL containing 50 pmol of each primer, 0.4 mM deoxyribonucleotide and 1.0 unit Pfu polymerase (Stratagene) in the corresponding buffer. The primary PCR reaction amplified the two separate fragments by 30 cycles, each cycle comprising 40 seconds at 94°C, 40 seconds at 50°C, 60 seconds at 72°C and an extension step at 72°C for 10 min. The second PCR reaction amplified the recombinant fragment in 12 cycles using the same conditions reported above. The ~~full-lengthed~~ full-length

product was cloned in the EcoRI site of the cloning vector pCR2.1 (Fig. 24A) and sequenced as noted above. This plasmid is referred to as pCR2.1-Pv-FRIL.

Please replace the paragraph at page 88, lines 9-14, with the following amended paragraph:

Cells were analyzed for their DNA content by staining with propidium iodide (Sigma). The cells were cultured in *ex vivo* cultures as described, for ~~3,6,10, and 13 days~~ 3, 6, 10, and 13 days as indicated. At each time point, the cells were collected, resuspended to a final concentration of 0.1-1x$10^6$ cells/mL, and incubated with 0.1% Triton X 100 (Sigma) for 20 minutes on ice. 50 mg/mL propidium iodide (PI) were added before analysis. Flow cytometeric analyses were performed using FACSort (Becton Dickinson, San Jose, CA).

Please replace the paragraph at page 89, lines 22-23, with the following amended paragraph:

Dl-FRIL maintains but does not expand CB ~~CD34$^+$ progenitors~~ CD34$^+$ progenitors in suspension culture

Please replace the paragraph at page 90, lines 14-15, with the following amended paragraph:

Dl-FRIL maintains the expansion capacity of ~~CD34$^+$ progenitors~~ CD34$^+$ progenitors up to 2 weeks in *ex vivo* culture

Please replace the paragraph bridging pages 99 and 100, with the following amended paragraph:

A reduction in cell number and a corresponding increase in the frequency of progenitors in cultures containing Dl-FRIL in the presence of potent stimulators are consistent with our hypothesis that Dl-FRIL can prevent cytokine-induced proliferation and differentiation of

progenitors. Table 8 below shows the relative decrease of MNC in Dl-FRIL-containing cultures compared to controls and the relative increase in progenitor frequency of progenitors. The total number of progenitors was reduced as expected (progenitors are at varying stages of differentiation [[□]] - no direct correlation between progenitor number and MNC would be expected).

Please replace the paragraph at page 101, lines 16-23, with the following amended paragraph:

The upper limits of Dl-FRIL toxicity were next explored by injecting a single bolus intraperitoneal injection of Dl-FRIL (to accommodate 1 mL volume) at 500 mg/kg and monitored the survival of mice for 48 hours. Of the four BALB/c mice receiving this treatment (2 males and 2 females, aged 5 months), only 1 mouse (a male) survived 48 hours. The surviving mouse's weight decreased by approximately 15% in the first 2 [[day]] days and returned to normal by day 4. The surviving mouse's blood counts were in the normal range 3 days after injection of FRIL. The results demonstrate that even a very large dose of Dl-FRIL is not completely toxic.

Please replace the paragraph at page 104, lines 9-20, with the following amended paragraph:

A dose regimen was established to determine whether FRIL protects mice from death resulting from hematopoietic toxicity of Ara-C and Dox. This murine 5-FU chemoprotection model is based on studies showing that a single dose of 5-FU (150 mg/kg) resulted in >90% reduction of bone marrow cellularity but had limited cytotoxic effect on stem cells (Lerner and Harrison, *Exp. Hematol.* 18:114-118, 1990). This finding was consistent with the understanding that stem cells reside in the bone marrow in predominantly a quiescent state. Bone marrow cellularity in these mice was restored after 2 weeks by the recruitment of the dormant progenitors and responsive stem cells that escaped toxicity of 5-FU. Administration of a second

dose of 5-FU (also at 150 mg/kg) 3 [[□]] ± 7 days after the initial dose killed those stem cells and progenitors recruited into S-phase in response to the first treatment of 5-FU (Lerner and Harrison, *supra*).

Please replace the paragraph bridging pages 104 and 105, with the following amended paragraph:

de Haan et al. (*Blood* 87:4581-4588., 1996) applied this model to test whether prophylactic treatment of mice with hematopoietic regulators, pegylated SCF + IL11, could expand the stem cell and primitive progenitor compartments and better protect mice from death by 5-FU induced hematopoietic toxicity. These experiments demonstrated that although SCF + IL11 pretreatment could accelerate hematopoietic recovery after it was underway by 4 days [[□]] ± 5 days when compared to controls (from approximately 11 days to 7 days for 40% survival, the SCF + IL11 cytokine pretreatment strategy did not rescue mice from death when the second dose of 5-FU was administered in the critical first week when stem cells are ablated (de Haan et al. (*supra*).

Please replace the paragraph at page 106, lines 6-7, with the following amended paragraph:

Optimization of the dose regiment of a FRIL family member
to protect mice from [[5-Fu]] 5-FU induced death

Please replace the paragraph at page 106, lines 24-29, with the following amended paragraph:

The five doses of Dl-FRIL are 0, 5, 50, 500, and 5,000 μg/kg. The four dose regimens of Dl-FRIL will be -2hour; -1day and -2hour; -2day, -1day, and -2hour; -3day, -2day, -1day, and -2hour prior to 5-FU treatment. The two maintenance regimens are either daily x 7 day (-2hour to day 7) or every other [[d]] day (days 0, 2, 4, 6). Thus, one group of mice will receive a dose of

Dl-FRIL daily for 7 days; while the second group will receive a dose of Dl-FRIL every other day for 7 days.

Please replace the paragraph at page 107, lines 10-14, with the following amended paragraph:

Initial dose regimens of cytarabine (Ara-C) and doxorubicin are as follows: Doxorubicin [[□]] - 14 mg/kg as single bolus i.p. injection (Grzegorzewski et al., *J.Exp.Med.* 180:1047-1057, 1994); Ara-C - 300 mg/kg at time as an i.p. injection at 0 and 12 hours (Paukovits et al., *Blood* 77:1313-1319, 1991). Further studies are based on targeted clinical ~~indication~~ indication.

Please replace the paragraph bridging pages 108-109, with the following amended paragraph:

Hypersensitivity studies in guinea pigs are performed to test for any adverse immunologic reactions. To do this, fifteen guinea pigs (5 FRIL, 5 DNCB positive control, 5 saline negative control) are used. A FRIL family member is intradermally injected at 0.1 mL. Daily clinical observations at site for redness and edema are compared to the DNCB positive control. The FRIL guinea pigs are challenged at [[at]] 2 weeks with 0.05 mL of the FRIL family member, and daily clinical observations are made.

Please replace the paragraph at page 112, lines 22-23, with the following amended paragraph:

Cord blood mononuclear cells were isolated by Ficoll-Paque, bead selected, and plated in ~~MethoCult□~~ MethoCult®, StemCell Technologies, Vancouver, BC, Canada).

Please replace the paragraph at page 114, lines 17-26, with the following amended paragraph:

Cells that retained Dl-FRIL-beads after overnight incubation on a rocker in the cold room (Dl-FRIL$^{++}$ cells) were observed as single cells or as clumps of bead-bound cells. These clumps could not be disrupted either by mechanical means or by elution with competing sugars, mannose or mannose derivatives (data not shown). From studies to characterize the carbohydrate-binding properties of Dl-FRIL, $\alpha$, $\alpha$-trehalose demonstrated a 3.6-fold greater potency than mannose and a 1.6- to 2.1-fold greater potency than $\alpha$-methyl $\alpha$-D-mannoside derivatives that were tested (Mo et al., ~~Glycobiology~~ *Glycobiology* 9:173-179, 1999). Incubation of clumped Dl-FRIL-bead bound cells with 100 mM Trehalose effectively disrupted the clumped cells and removed most of the Dl-FRIL-beads from cells.

Please replace the paragraph at page 118, lines 22-29, with the following amended paragraph:

_____DC are derived from CD34$^{+}$ progenitors in the bone marrow of humans. The cytokines GM-CSF, TNF-$\alpha$, and Flt3 ligand (FL) influence DC development (Banchereau and Steinman, *supra*; Pulendran et al., *J. Immunol.* 159:2222-2231, 1997). Injection of FLT3-Ligand in mice dramatically increases the number of DC (Pulendran et al., *supra*). FRIL interacts with the Flt3 receptor on DC, and FRIL-beads capture cells with the dendritic phenotype of CD11b and CD11c. Selecting dendritic cells with FRIL-beads from human bone marrow, peripheral blood, or cord blood allows the efficient and effective isolation of DC for clinical use.

Please replace the paragraph at page 119, lines 21-25, with the following amended paragraph:

Other legume- or bulb-derived lectins can also ~~delivery~~ deliver small molecule drugs to specific cell populations. For example, the lectins PHA and ConA both bind to CD3-T cell receptor complex and the FC-gamma receptor (CD32) (Leca et al. *Scand. J. Immunol.* 23:535-544,

1986); UDA binds the Vβ domain of the T cell receptor (Galelli et al., *J. Immunol.* 151:1821-1831, 1993).

Please replace the Abstract at page 129, lines 7-12, with the following amended paragraph:

Disclosed [[is]] <u>are</u> the FRIL family of progenitor cell preservation factors and nucleic acids encoding the same. FRIL family members preserve progenitor cells both *in vivo* and *ex vivo*. FRIL family members find use as therapeutics for alleviating and/or reducing the hematopoietic progenitor cell-depleting activity of many cancer therapeutics. FRIL family members are also useful for isolating rare, primitive progenitor cells.

Please replace the last-filed Sequence Listing with the attached Sequence Listing (*see*, **Attachment A**).